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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:17:00 ON 15 JAN 2002

=> fil reg

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 0.15 | 0.15 |

FILE 'REGISTRY' ENTERED AT 14:17:09 ON 15 JAN 2002
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STRUCTURE FILE UPDATES: 14 JAN 2002 HIGHEST RN 383122-99-4
DICTIONARY FILE UPDATES: 14 JAN 2002 HIGHEST RN 383122-99-4

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when
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Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=>

Uploading 779116b.str

L1 STRUCTURE UPLOADED

=> d

L1 HAS NO ANSWERS
L1 STR

N

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Structure attributes must be viewed using STN Express query preparation.

=> s 11 sss sam

SAMPLE SEARCH INITIATED 14:17:49 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 12904 TO ITERATE

7.7% PROCESSED 1000 ITERATIONS 2 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.03

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 251289 TO 264871
PROJECTED ANSWERS: 212 TO 820

L2 2 SEA SSS SAM L1

=> s 11 full

FULL SEARCH INITIATED 14:17:57 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 260128 TO ITERATE

100.0% PROCESSED 260128 ITERATIONS 70 ANSWERS
SEARCH TIME: 00.00.09

L3 70 SEA SSS FUL L1

=> fil caplus

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 140.54 | 140.69 |

FILE 'CAPLUS' ENTERED AT 14:18:11 ON 15 JAN 2002
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FILE COVERS 1907 - 15 Jan 2002 VOL 136 ISS 3
FILE LAST UPDATED: 14 Jan 2002 (2002C114/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

CAplus now provides online access to patents and literature covered in CA from 1907 to the present. Bibliographic information and abstracts were added in 2001 for over 3.8 million records from 1907-1966.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

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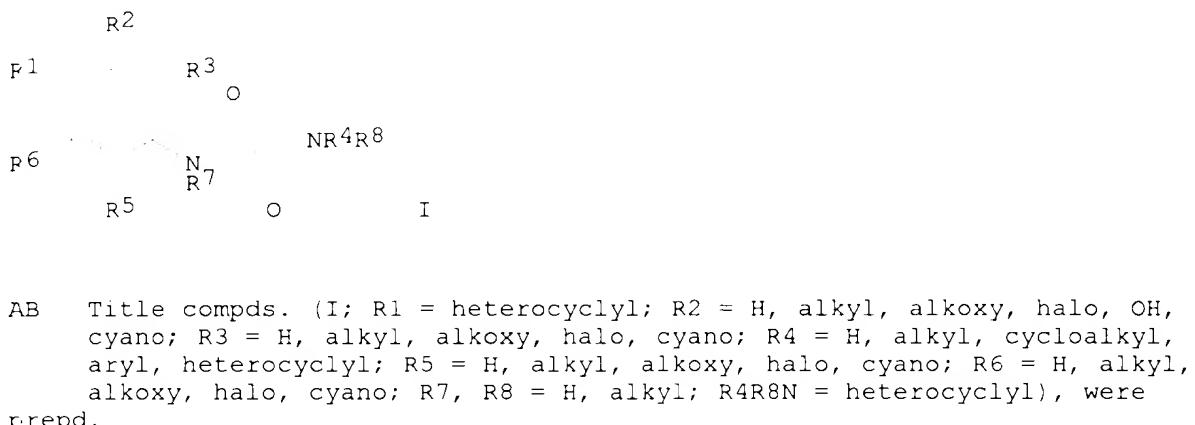
=> s 13 full

L4 8 L3

=> d 14 1-8 ibib abs hitstr

L4 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:631913 CAPLUS
DOCUMENT NUMBER: 135:195556
TITLE: Preparation of azolylphenyl oxamides as inosine monophosphate dehydrogenase (IMPDH) inhibitors
INVENTOR(S): Broadhurst, Michael John; Hill, Christopher Huw; Hurst, David Nigel; Jones, Philip Stephen; Kay, Paul Brittain; Kilford, Ian Reginald; Mckinnell, Robert Murray
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: Eur. Pat. Appl., 256 pp.
CODEN: EPWWDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| EP 1127883 | A2 | 20010829 | EP 2001-103521 | 20010216 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| NO 2001000900 | A | 20010827 | NO 2001-900 | 20010222 |
| CN 1310179 | A | 20010829 | CN 2001-104906 | 20010223 |
| JP 2001261663 | A2 | 20010926 | JP 2001-51064 | 20010226 |
| PRIORITY APPLN. INFO.: | | | GB 2000-4392 | A 20000224 |
| | | | GB 2000-15877 | A 20000628 |
| | | | GB 2000-20322 | A 20000817 |



Thus, 1,1-dimethyl-3-(4-nitrophenoxy)propylamine (prepn. given) was coupled with N-[3-methoxy-4-(5-oxazolyl)phenyl]oxamic acid in the presence

of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide and 1-hydroxy-7-azabenzotriazole to give N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-(1,1-dimethyl-3-(4-nitrophenoxy)propyl)oxalamide. Tested I inhibited IMPDH with IC₅₀ = 0.010-0.277 .μ.M. I can be used for treating immune mediated

conditions or diseases, viral diseases, bacterial diseases, parasitic diseases, inflammation, inflammatory diseases, hyperproliferative vascular diseases, tumors, and cancer.

IT 267405-69-6P 357179-57-8P 357179-58-9P
357179-59-0P 357179-69-2P 357179-71-6P
357179-74-9P 357179-88-5P 357180-70-2P
357180-82-6P 357180-83-7P 357180-84-8P
357180-85-9P 357180-86-0P 357180-95-1P
357180-96-2P 357180-97-3P 357180-98-4P
357180-99-5P 357181-00-1P 357181-01-2P
357181-02-3P 357181-03-4P 357181-36-3P
357181-37-4P 357181-38-5P 357181-40-9P
357181-41-0P 357181-42-1P 357181-43-2P
357181-44-3P 357181-45-4P 357181-46-5P
357181-47-6P 357181-48-7P 357181-49-8P
357181-50-1P 357181-51-2P 357181-52-3P
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357183-19-8P

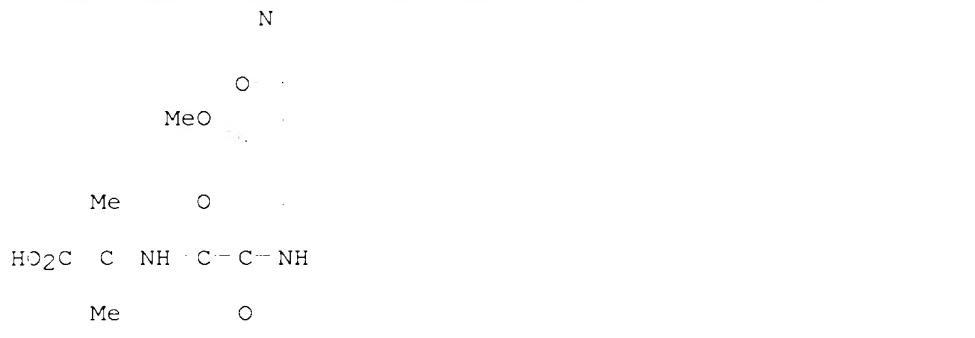
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of azolylphenyl oxamides as inosine monophosphate dehydrogenase

(IMPDH) inhibitors)

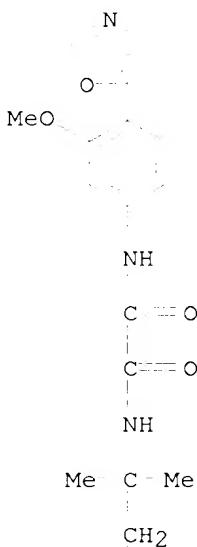
RN 267405-69-6 CAPLUS

CN Alanine, N-[3-methoxy-4-(5-oxazolyl)phenyl]-2-oxoglycyl-2-methyl- (9CI)
(CA INDEX NAME)

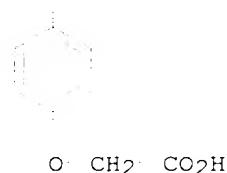


RM 357179-57-8 CAPLUS
 CN Acetic acid,
 [4-[2-[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]oxoacetyl]amin
 o]-2-methylpropyl]phenoxy]- (9CI) (CA INDEX NAME)

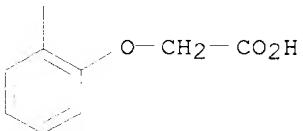
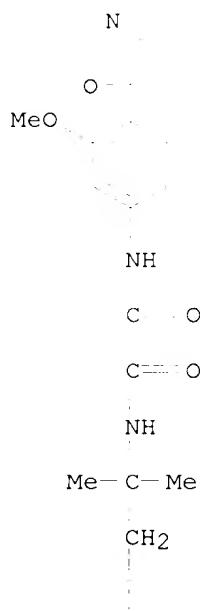
PAGE 1-A



PAGE 2-A



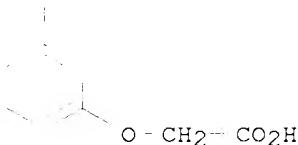
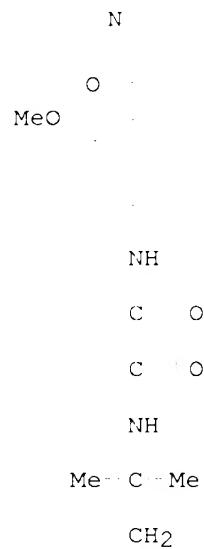
RM 357179-58-9 CAPLUS
 CN Acetic acid,
 [2-[2-[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]oxoacetyl]amin
 o]-2-methylpropyl]phenoxy]- (9CI) (CA INDEX NAME)



RN 357179-59-0 CAPLUS

CN Acetic acid,

[3-[2-[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]oxoacetyl]amino]-2-methylpropyl phenoxyacetic acid] (9CI) (CA INDEX NAME)



RN 357179-69-2 CAPLUS

CN Benzoic acid,

4-[2-[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]oxoacetyl]amino]-2-methylpropionic acid (9CI) (CA INDEX NAME)

N

O

MeO

NH

C O

C O

NH

Me - C - Me

CH₂CO₂H

RN 357179-71-6 CAPLUS

CN Benzoic acid,

3-[2-[[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]oxoacetyl]amino]-2-methylpropyl]-(9CI) (CA INDEX NAME)

N



NH

C O

C O

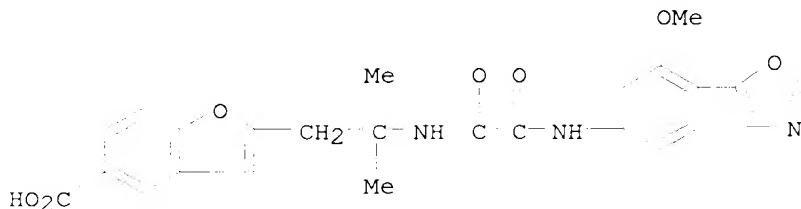
NH

Me C Me

CH₂CO₂H

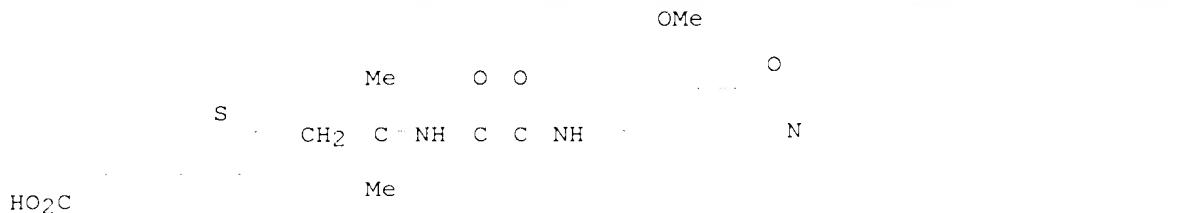
RN 357179-74-9 CAPLUS

CN 5-Benzofurancarboxylic acid, 2-[2-[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]oxoacetyl]amino]-2-methylpropyl- (9CI) (CA INDEX NAME)



RN 357179-88-5 CAPLUS

CN Benzo[b]thiophene-5-carboxylic acid, 2-[2-[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]oxoacetyl]amino]-2-methylpropyl- (9CI) (CA INDEX NAME)

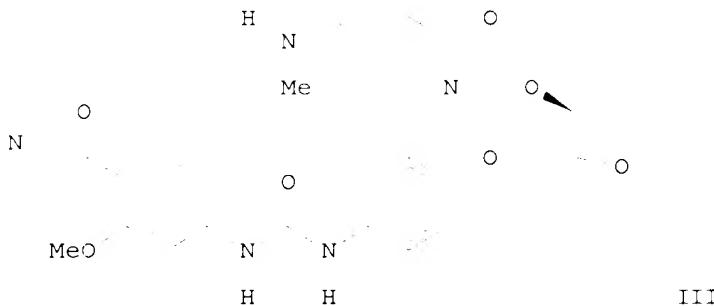
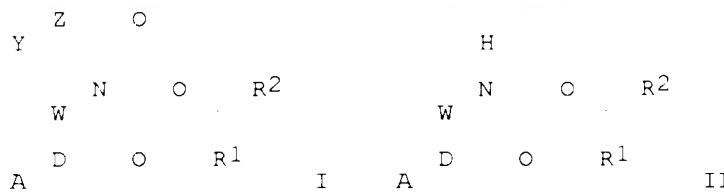


RN 357180-70-2 CAPLUS
 CN Benzoic acid,
 4-[[4-[2-[[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]oxoacetyl]amino]-2-methylpropyl]phenyl]amino]carbonyl- (9CI) (CA INDEX NAME)

u
 CN Benzoic acid,
 4-[3-[[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]oxoacetyl]amino]-3-methylbutoxy]- (9CI) (CA INDEX NAME)
 => d 14 2-8 ibib abs hitstr

L4 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:12455 CAPLUS
 DOCUMENT NUMBER: 134:86041
 TITLE: Preparation of carbamate prodrugs for inhibition of inosine monophosphate dehydrogenase (IMPDH)
 INVENTOR(S): Stamos, Dean P.; Bethiel, Randy S.
 PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
 SOURCE: PCT Int. Appl., 63 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|------------------|-----------------|------------|
| WO 2001000622 | A1 | 20010104 | WO 2000-US17400 | 20000623 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| PRIORITY APPLN. INFO.: | | | US 1999-141102 | P 19990625 |
| OTHER SOURCE(S): | | MARPAT 134:86041 | | |
| GI | | | | |



AB Carbamate prodrugs I [W = (un)substituted monocyclic or bicyclic, (un)satd. or arom. ring system consisting of 5-6 members per ring (optionally heterocyclic); D = NR₃CONR₃, CONR₃, NR₃CO, NR₃COCR₄:CR₄ where each R₃ = H, (un)substituted alkyl, alkenyl or alkynyl; R₄ = R₃, (un)substituted alkyl, alkenyl or alkenyl attached via O, OCO, S, SO, SO₂, SCO, NR₃, or NR₃CO; A = W, alkyl, alkenyl, or alkynyl where A optionally comprises up to 2 substituents wherein: the first of said substituents is R₅ or W, and the second substituent, if present, is R₅; R₅ = (un)substituted 1,2-methylenedioxy, 1,2-ethylenedioxy, alkyl, alkenyl or alkynyl or (CH₂)_nW₁; W₁ = halo, CN, NO₂, CF₃, OH, alkoxy, etc.; n = 0-2; Y = NR₆; R₆ = H, (un)substituted alkyl, alkenyl, alkynyl, aryl or alkylaryl and any NR₆, taken together with the nitrogen and a carbon adjacent to the nitrogen, optionally forms a 5-7 membered ring, wherein said ring optionally contains up to 3 addnl. heteroatoms; Z = (un)substituted alkyl, alkenyl, alkynyl, aryl-alkyl, -alkenyl or -alkynyl, wherein up to 3 carbon atoms may be replaced with O, S, SO, SO₂, or NR₆, wherein up to 3 CH₂ groups may be replaced with CO; R₁ = (un)substituted alkyl; R₂ = H, CF₃, alkyl, alkyl-W, W, or R₁ and R₂ together form a ring as defined in W], that on metab. convert to active inhibitors (formula II) of the IMPDH enzyme in vivo, were prep'd. Thus, III.cndot.HCl was prep'd. from methylaminobutyric acid in seven steps. I and pharmaceutical compns. thereof are particularly well suited for activation and subsequent inhibition of the IMPDH enzyme activity. The rate of absorption of I via oral uptake of the prodrugs was dependent on the nature of substituents Z and Y, as well as the pH, with AUC values ranging from <1 to 5 mg.cndot.hr/mL. Consequently, I may be advantageously used as therapeutic agents for IMPDH-mediated processes, e.g., cell proliferation (antitumor agents), and viral replication (antiviral agents).

IT **317345-76-9P**

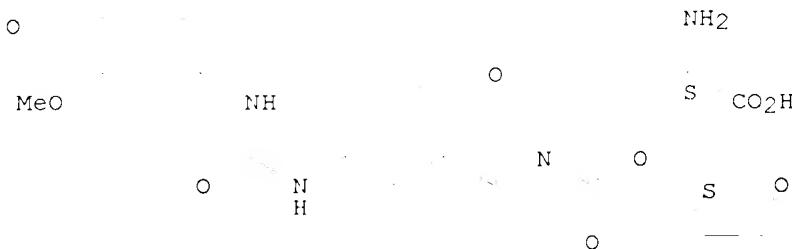
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses) (prepn. and biol. activity of N,N'-diphenylurea prodrugs of carbamate inhibitors of IMPDH)

RN 317345-76-9 CAPLUS

CN L-Glutamine,
 N-[[3-[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]carbonyl]amino
]phenyl]methyl]-N-[[[(3S)-tetrahydro-3-furanyl]oxy]carbonyl]-,
 monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

N



● HCl

REFERENCE COUNT:

5

REFERENCE(S):
 1988,

(1) Beylin, V; JOURNAL OF HETEROCYCLIC CHEMISTRY

V25(1), P97 CAPLUS
 (2) Kahns, A; 1991, 6, P483 CAPLUS
 (3) Kahns, A; INT J PHARM 1991, V71(1-2), P31 CAPLUS
 (4) Sharma, S; JOURNAL OF MEDICINAL CHEMISTRY 1989,
 V32(2), P357 CAPLUS
 (5) Vertex Pharmaceuticals Incorporated; WO 9740028 A
 1997 CAPLUS

L4 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:688087 CAPLUS

DOCUMENT NUMBER: 133:261545

TITLE: Inosine-5'-monophosphate dehydrogenase (IMPDH)
 inhibitors, their preparation, and their therapeutic
 use

INVENTOR(S): Stamos, Dean; Trudeau, Martin; Bethiel, Scott; Badia,
 Michael; Saunders, Jeffrey

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 89 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|---|----------|-----------------|------------|
| WO 2000056331 | A1 | 20000928 | WO 2000-US7129 | 20000317 |
| W: | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID,
IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG,
SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| PRIORITY APPLN. INFO.: | | | US 1999-125507 | P 19990319 |

OTHER SOURCE (S):

MARPAT 133:261545

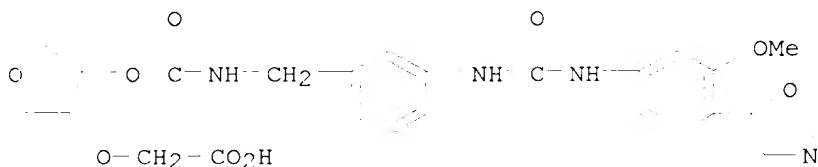
AB Compds. and pharmaceutical compns. are provided which inhibit IMPDH. The compds. and pharmaceutical compns. of the invention are particularly well suited for inhibiting IMPDH activity and consequently, may be used as therapeutic agents for IMPDH-mediated processes. The invention also relates to methods for inhibiting the activity of IMPDH using the compds. of the invention and related compds.

IT 297728-82-6 297729-82-9 297729-83-0

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inosine monophosphate dehydrogenase inhibitors, prepns., and therapeutic use)

RN 297728-82-6 CAPLUS

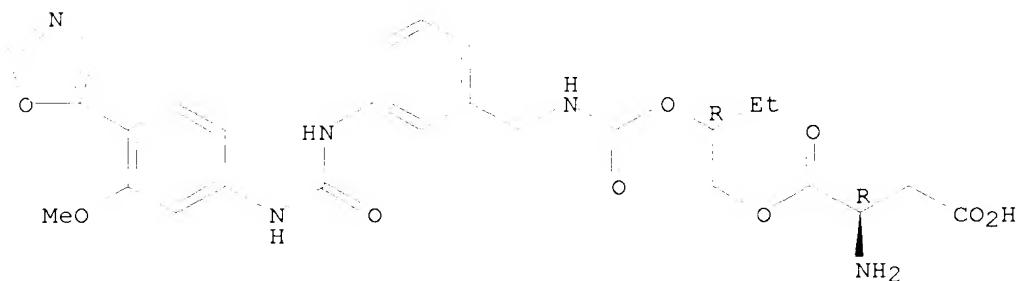
CN Acetic acid, [[tetrahydro-4-[[[[[3-[[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]carbonyl]amino]phenyl]methyl]amino]carbonyl]oxy]-3-furanyl]oxy]- (9CI) (CA INDEX NAME)



RN 297729-82-9 CAPLUS

CN D-Aspartic acid, 1-[(2R)-2-[[[[[3-[[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]carbonyl]amino]phenyl]methyl]amino]carbonyl]buty 1] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

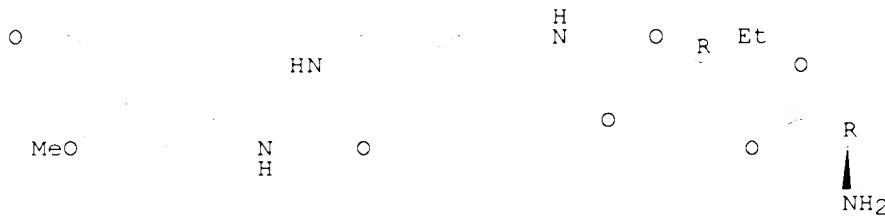


RN 297729-83-0 CAPLUS

CN D-Glutamic acid, 1-[(2R)-2-[[[[[3-[[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]carbonyl]amino]phenyl]methyl]amino]carbonyl]buty 1] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

N

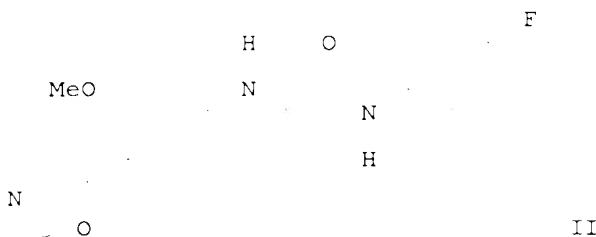
—CO₂H

REFERENCE COUNT: 1
 REFERENCE(S): (1) Vertex Pharmaceuticals Incorporated; WO 9740028
 A1

1997 CAPLUS

L4 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:314692 CAPLUS
 DOCUMENT NUMBER: 132:334449
 TITLE: Preparation of N-[4-(5-oxazolyl)phenyl] amides as
 novel inhibitors of IMPDH enzyme
 INVENTOR(S): Gu, Henry H.; Dhar, T. G. Murali; Iwanowicz, Edwin
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
 SOURCE: PCT Int. Appl., 99 pp.
 CODEN: PIIXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|-------------------|-----------------|------------|
| WO 2000026197 | A1 | 20000511 | WO 1999-US24889 | 19991022 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, UA, UG, UE, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1127054 | A1 | 20010829 | EP 1999-960145 | 19991022 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO | | | | |
| PRIORITY APPLN. INFO.: | | | US 1998-106180 | P 19981029 |
| | | | WO 1999-US24889 | W 19991022 |
| OTHER SOURCE(S): | | MARPAT 132:334449 | | |
| GI | | | | |



AB The title compds. ZJKLX [I; Z = (un)substituted monocyclic or bicyclic ring system contg. up to 4 heteroatoms selected from N, O, and S; J = NR₇,

CO; K = NR₇, CO, CHR₉; L = a single bond, CO, CR₁₀R₁₁, etc.; X = alkyl, alkenyl, cycloalkylalkyl, etc.; R₇ = H, alkyl, alkenyl, etc.; R₉ = H, alkyl, alkenyl, etc.; R₁₀, R₁₁ = H, F, Cl, etc.], useful in treating or preventing IMPDH assoccd. disorders, such as transplant rejection and autoimmune disease, were prepnd. E.g., a multi-step synthesis of gycinamide II was given. Compds. I are effective at 0.1-500 mg/kg/day.

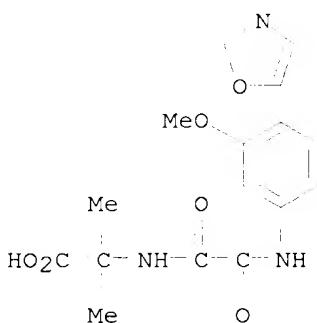
IT **267405-69-6P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-[4-(5-oxazolyl)phenyl] amides as novel inhibitors of IMPDH enzyme)

RN 267405-69-6 CAPLUS

CN Alanine, N-[3-methoxy-4-(5-oxazolyl)phenyl]-2-oxoglycyl-2-methyl- (9CI)
(CA INDEX NAME)



IT **267406-37-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of N-[4-(5-oxazolyl)phenyl] amides as novel inhibitors of

IMPDH

enzyme)

RN 267406-37-1 CAPLUS

CN Propanoic acid, 3-[(3-methoxy-4-(5-oxazolyl)phenyl)amino]-3-oxo- (9CI)
(CA INDEX NAME)

N

O

MeC

HO₂C CH₂ C—NH

O

REFERENCE COUNT:

3

REFERENCE(S):

- (1) Diana; US 4861791 A 1989 CAPLUS
- (2) Djuric; US 5073562 A 1991 CAPLUS
- (3) Goldstein; US 5334604 A 1994 CAPLUS

L4 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:314540 CAPLUS

DOCUMENT NUMBER: 132:334477

TITLE: Preparation of compounds derived from an amine
nucleus

as inhibitors of IMPDH enzyme

INVENTOR(S): Liu, Chunjian; Dhar, T. G. Murali; Gu, Henry H.;
Iwanowicz, Edwin J.; Leftheris, Katerina; Pitts,
William John

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 191 pp.

CODEN: PIXXD2

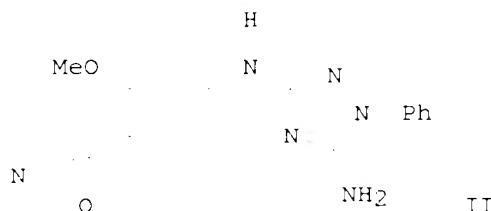
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|-------------------|-----------------|------------|
| WO 2000025780 | A1 | 20000511 | WO 1999-US24825 | 19991022 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1126843 | A1 | 20010829 | EP 1999-955142 | 19991022 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO | | | | |
| PRIORITY APPLN. INFO.: | | | US 1998-106186 | P 19981029 |
| | | | WO 1999-US24825 | W 19991022 |
| OTHER SOURCE(S): | | MARPAT 132:334477 | | |
| GI | | | | |



AB The title compds. XN(R)BD [I; X = (un)substituted monocyclic or bicyclic ring system optionally contg. up to 4 heteroatoms selected from N, O, and S; R = H, alkyl; B = (un)substituted monocyclic or bicyclic ring system optionally contg. up to 4 heteroatoms selected from N, O, and S; D = (un)substituted monocyclic or bicyclic ring system optionally contg. up

to 4 heteroatoms selected from N, O, and S], useful in treating or preventing

IMPDH (inosine-5'-monophosphate dehydrogenase) mediated diseases, such as transplant rejection and autoimmune diseases, were prepd. E.g., a multi-step synthesis of triazole II was given. Compds. I are effective

at

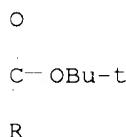
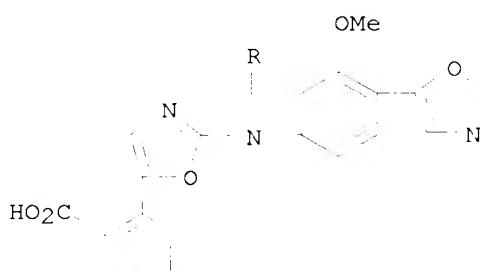
0.1-500 mg/kg/day.

IT **267648-02-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prep. of compds. derived from an amine nucleus as inhibitors of IMPDH enzyme)

PN 267648-02-2 CAPLUS

CN Benzoic acid, 2-[2-[[[(1,1-dimethylethoxy)carbonyl] [3-methoxy-4-(5-oxazolyl)phenyl]amino]-5-oxazolyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

1

REFERENCE(S):

(1) Knox; US 5247083 A 1993 CAPLUS

L4 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:268526 CAPLUS

DOCUMENT NUMBER: 132:288797

TITLE: Inosine 5'-monophosphate dehydrogenase (IMPDH) inhibitor preparation for therapeutic use

INVENTOR(S): Armistead, David M.; Badia, Michael C.; Bemis, Guy W.;

Bethiel, Randy S.; Frank, Catharine A.; Novak, Perry

PATENT ASSIGNEE(S): M.; Ronkin, Steven M.; Saunders, Jeffrey O.
 SOURCE: Vertex Pharmaceuticals, Incorporated, USA
 U.S., 22 pp., Cont.-in-part of U.S. 5,807,876.
 CODEN: USXXAM

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| US 6054472 | A | 20000425 | US 1997-832165 | 19970402 |
| US 5307876 | A | 19980915 | US 1996-636361 | 19960423 |
| WO 9740028 | A1 | 19971030 | WO 1997-US6623 | 19970421 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN,
YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB,
GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN,
ML, MR, NE, SN, TD, TG | | | | |
| AU 9726785 | A1 | 19971112 | AU 1997-26785 | 19970421 |
| AU 723730 | B2 | 20000907 | | |
| EP 902782 | A1 | 19990324 | EP 1997-918759 | 19970421 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO | | | | |
| CN 1019929 | A | 19990616 | CN 1997-194856 | 19970421 |
| BR 9708735 | A | 19990803 | BR 1997-8735 | 19970421 |
| JP 2001509132 | T2 | 20010710 | JP 1997-538234 | 19970421 |
| NO 9804917 | A | 19981223 | NO 1998-4917 | 19981022 |
| KR 2000010580 | A | 20000215 | KR 1998-708454 | 19981022 |
| US 1996-636361 A2 19960423
US 1997-801780 A2 19970214
US 1997-832165 A 19970402
WO 1997-US6623 W 19970421 | | | | |

PRIORITY APPLN. INFO.:

OTHER SOURCE(S): MARPAT 132:288797

AB The invention relates to a novel class of compds. which are IMPDH inhibitors. This invention also relates to pharmaceutical compns. comprising these compds. The compds. and pharmaceutical compns. of the invention are particularly well suited for inhibiting IMPDH activity and consequently may be used as therapeutic agents for IMPDH-mediated processes. The invention also relates to methods for inhibiting the activity of IMPDH using the compds. of the invention and related compds.

IT 198820-33-6 198820-44-9 198820-62-1

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (inosine monophosphate dehydrogenase inhibitor prepn. for therapeutic use)

RN 198820-33-6 CAPLUS

CN Benzenepropanoic acid, 3-[[[[4-(5-oxazolyl)phenyl]amino]carbonyl]amino]-(9CI) (CA INDEX NAME)

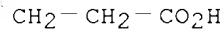
N

O

NH

C=O

NH



RN 198820-44-9 CAPLUS

CN Benzeneacetic acid, 3-[[[[4-(5-oxazolyl)phenyl]amino]carbonyl]amino]-
(9CI) (CA INDEX NAME)

N

O

NH

C=O

NH



RN 198820-62-1 CAPLUS

CN Benzeneacetic acid,
3-[[[[3-chloro-4-(5-oxazolyl)phenyl]amino]carbonyl]ami
no]- (9CI) (CA INDEX NAME)

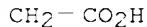
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NH

C O

NH



REFERENCE COUNT:

13

REFERENCE(S):

- (1) Anon; US 4048333 1977 CAPLUS
- (2) Anon; WO 9401105 1994 CAPLUS
- (3) Anon; WO 9412184 1994 CAPLUS
- (4) Anon; US 5380879 1995 CAPLUS
- (5) Anon; US 5444072 1995 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:717901 CAPLUS

DOCUMENT NUMBER: 128:3680

TITLE: Preparation of arylreas and related compounds as inhibitors of inosine 5'-monophosphate dehydrogenase.

INVENTOR(S): Armistead, David M.; Badia, Michael C.; Bemis, Guy

W.;

Bethiel, Randy S.; Frank, Catharine A.; Novak, Perry M.; Ronkin, Steven M.; Saunders, Jeffrey O.

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Inc., USA

SOURCE: PCT Int. Appl., 93 pp.

CODEN: PIKKD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9740028 | A1 | 19971030 | WO 1997-US6623 | 19970421 |
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| RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 5807876 | A | 19980915 | US 1996-636361 | 19960423 |
| US 6054472 | A | 20000425 | US 1997-832165 | 19970402 |
| AU 9726785 | A1 | 19971112 | AU 1997-26785 | 19970421 |
| AU 723730 | B2 | 20000907 | | |
| EP 902782 | A1 | 19990324 | EP 1997-918759 | 19970421 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| BR 9708735 | A | 19990803 | BR 1997-8735 | 19970421 |

| | | | | |
|------------------------|----|----------|----------------|------------|
| JP 2001509132 | T2 | 20010710 | JP 1997-538234 | 19970421 |
| NO 9804917 | A | 19981223 | NO 1998-4917 | 19981022 |
| PRIORITY APPLN. INFO.: | | | US 1996-636361 | A 19960423 |
| | | | US 1997-801780 | A 19970214 |
| | | | US 1997-832165 | A 19970402 |
| | | | WO 1997-US6623 | W 19970421 |

OTHER SOURCE(S): MARPAT 128:3680

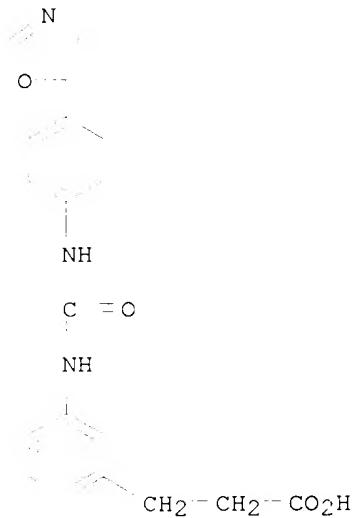
AB ANHDNHB [A = (substituted) alkyl, alkenyl, alkynyl; B = (unsatd.) (substituted) mono- or bicyclic ring contg. 1 to ≤ 4 heteroatoms; D = CO, CS, SO₂], were prep'd. Thus, 4-(5-oxazolyl)aniline and PhCH₂NCO were stirred overnight in CH₂Cl₂ to give N-benzyl-N'-(4-(5-oxazolyl)phenyl)urea. Several title compds. inhibited IMPDH with $K_i = 0.01\text{--}5$ nM.

IT 198820-33-6 198820-44-9 198820-62-1

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (prepn. of arylreas and related compds. as inhibitors of IMP dehydrogenase)

RN 198820-33-6 CAPLUS

CN Benzenepropanoic acid, 3-[[[[4-(5-oxazolyl)phenyl]amino]carbonyl]amino]-(9CI) (CA INDEX NAME)



RN 198820-44-9 CAPLUS

CN Benzenepropanoic acid, 3-[[[[4-(5-oxazolyl)phenyl]amino]carbonyl]amino]-(9CI) (CA INDEX NAME)

N

C

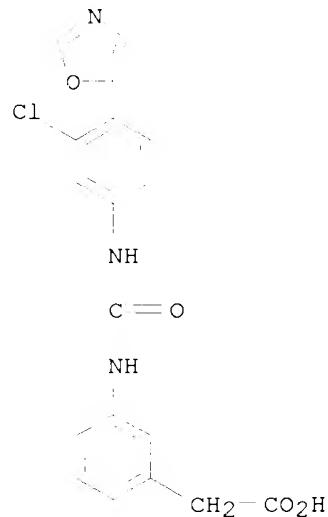
NH

C=O

NH

CH₂-CO₂H

RN 198820-62-1 CAPLUS
CN Benzeneacetic acid,
3-[[[3-chloro-4-(5-oxazolyl)phenyl]amino]carbonyl]ami
no]- (9CI) (CA INDEX NAME)



L4 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:507387 CAPLUS
DOCUMENT NUMBER: 109:107387
TITLE: Homogeneous fluoroassay methods employing fluorescent
background rejection and water-soluble rare earth
metal chelate fluorophores
INVENTOR(S): Wieder, Irwin; Hale, Ron L.
PATENT ASSIGNEE(S): Baxter Travenol Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

| | | | | |
|--|----|----------|----------------|-------------|
| WO 8707955 | A1 | 19871230 | WO 1987-US1407 | 19870615 |
| W: DK, FI, JP, NO | | | | |
| RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE | | | | |
| EP 272320 | A1 | 19880629 | EP 1987-905011 | 19870615 |
| EP 272320 | B1 | 19940323 | | |
| R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE | | | | |
| JP 01500458 | T2 | 19880216 | JP 1987-504676 | 19870615 |
| AT 103393 | E | 19940415 | AT 1987-905011 | 19870615 |
| CA 1309016 | A1 | 19921020 | CA 1987-539778 | 19870616 |
| DK 8800798 | A | 19880216 | DK 1988-798 | 19880216 |
| DK 172464 | B1 | 19980831 | | |
| FI 8800719 | A | 19880216 | FI 1988-719 | 19880216 |
| FI 93997 | B | 19950315 | | |
| FI 93997 | C | 19950626 | | |
| NO 8800684 | A | 19880412 | NO 1988-684 | 19880216 |
| US 5830769 | A | 19981103 | US 1996-732871 | 19961015 |
| US 6242268 | B1 | 20010605 | US 1998-184330 | 19981102 |
| PRIORITY APPLN. INFO.: | | | US 1986-875287 | A 19860617 |
| | | | US 1985-712774 | A2 19850318 |
| | | | US 1985-712779 | A2 19850318 |
| | | | EP 1987-905011 | A 19870615 |
| | | | WO 1987-US1407 | W 19870615 |
| | | | US 1993-35516 | B1 19930322 |
| | | | US 1994-338285 | B1 19941110 |
| | | | US 1996-732871 | A1 19961015 |

AB Homogeneous assays for detg. the extent of a specific binding reaction
can

be carried out on very dil. solns. using fluorescence measurements if a fluorescence measurement scheme is employed that is capable of rejecting short-lived background fluorescence. The fluorescent group must be a water-sol. rare earth metal chelate which is stable in extremely dil. aq. solns., i.e. it must have $\geq 10^{13}$ M-1. It must also have a fluorescent emission of long duration compared to the longest decay lifetime of ambient substances and must have a half-life of 0.01-50 ms. An energy transfer fluorescence enhancement assay for theophylline was carried out by allowing theophylline in a sample to compete for anti-theophylline antibody with a tracer, 2,6-bis[N,N-di(carboxymethyl)aminomethyl]-4-[4-(theophylline-8-butyramido)phenyl]pyridine Tb chelate (prepn. given). Theophylline could be detd. over the concn. range 5.4-540 ng/10 μ L, with an increase in the obsd. fluorescence of $\geq 400\%$.

IT **116241-45-3D**, antibody conjugates

RL: ANST (Analytical study)

(as fluorescence enhancer for fluorescence immunoassay)

RN 116241-45-3 CAPLUS

CN Octanoic acid, 8-oxo-8-[[3-oxo-3-[[4-(2-phenyl-5-oxazolyl)phenyl]amino]propyl]amino]- (9CI) (CA INDEX NAME)

Ph N

O

||

O

NH—C—CH2—CH2—NH—C—(CH2)6—CO2H

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---Logging off of STN---

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Executing the logoff script...

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| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|--|------------------|---------------|
| FULL ESTIMATED COST | 36.07 | 176.76 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | -4.96 | -4.96 |

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PASSWORD:

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| NEWS 1 | | | Web Page URLs for STN Seminar Schedule - N. America |
| NEWS 2 | Dec 17 | The CA Lexicon available in the CAPLUS and CA files | |
| NEWS 3 | Feb 06 | Engineering Information Encompass files have new names | |
| NEWS 4 | Feb 16 | TOXLINE no longer being updated | |
| NEWS 5 | Apr 23 | Search Derwent WPINDEX by chemical structure | |
| NEWS 6 | Apr 23 | PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA | |
| NEWS 7 | May 07 | DGENE Reload | |
| NEWS 8 | Jun 30 | Published patent applications (A1) are now in USPATFULL | |
| NEWS 9 | JUL 13 | New SDI alert frequency now available in Derwent's DWPI and DPCI | |
| NEWS 10 | Aug 23 | In-process records and more frequent updates now in MEDLINE | |
| NEWS 11 | Aug 23 | PAGE IMAGES FOR 1947-1966 RECORDS IN CAPLUS AND CA | |
| NEWS 12 | Aug 23 | Adis Newsletters (ADISNEWS) now available on STN | |
| NEWS 13 | Sep 17 | IMSworld Pharmaceutical Company Directory name change to PHARMASEARCH | |
| NEWS 14 | Oct 09 | Korean abstracts now included in Derwent World Patents Index | |
| NEWS 15 | Oct 09 | Number of Derwent World Patents Index updates increased | |
| NEWS 16 | Oct 15 | Calculated properties now in the REGISTRY/ZREGISTRY File | |
| NEWS 17 | Oct 22 | Over 1 million reactions added to CASREACT | |
| NEWS 18 | Oct 22 | DGENE GETSIM has been improved | |
| NEWS 19 | Oct 29 | AAASD no longer available | |
| NEWS 20 | Nov 19 | New Search Capabilities USPATFULL and USPAT2 | |
| NEWS 21 | Nov 19 | TOXCENTER(SM) - new toxicology file now available on STN | |
| NEWS 22 | Nov 29 | COPPERLIT now available on STN | |
| NEWS 23 | Nov 29 | DWPI revisions to NTIS and US Provisional Numbers | |
| NEWS 24 | Nov 30 | Files VETU and VETB to have open access | |
| NEWS 25 | Dec 10 | WPINDEX/WPIIDS/WPIX New and Revised Manual Codes for 2002 | |
| NEWS 26 | Dec 10 | DGENE BLAST Homology Search | |
| NEWS 27 | Dec 17 | WELDASEARCH now available on STN | |
| NEWS 28 | Dec 17 | STANDARDS now available on STN | |
| NEWS 29 | Dec 17 | New fields for DPCI | |
| NEWS 30 | Dec 19 | CAS Roles modified | |
| NEWS 31 | Dec 19 | 1907-1946 data and page images added to CA and CAplus | |

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CURRENT MACINTOSH VERSION IS V6.0 (ENG) AND V6.0J (JP),
AND CURRENT DISCOVER FILE IS DATED 07 AUGUST 2001

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FILE 'HOME' ENTERED AT 10:28:12 ON 15 JAN 2002

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| FULL ESTIMATED COST | 0.15 | 0.15 |

FILE 'REGISTRY' ENTERED AT 10:28:17 ON 15 JAN 2002
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DICTIONARY FILE UPDATES: 14 JAN 2002 HIGHEST RN 383122-99-4

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conducting SmartSELECT searches.

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Calculated physical property data is now available. See HELP PROPERTIES
for more information. See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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L1 STRUCTURE UPLOADED

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Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 10:28:58 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 4271 TO ITERATE

23.4% PROCESSED 1000 ITERATIONS 1 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 81504 TO 89336
PROJECTED ANSWERS: 1 TO 208

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=> s 11 full

FULL SEARCH INITIATED 10:29:05 FILE 'REGISTRY'
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=> fil caplus

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
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| FULL ESTIMATED COST | 140.54 | 140.69 |

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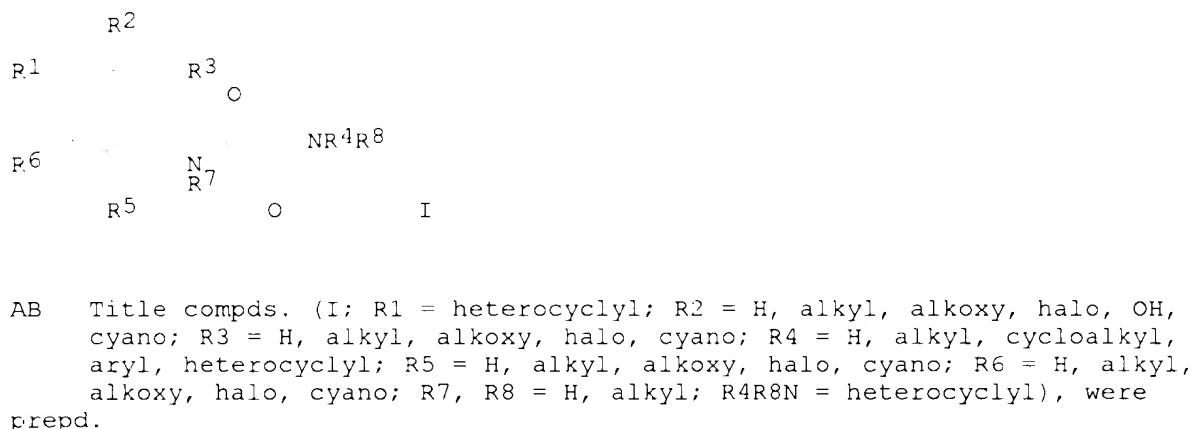
=> s 13 full

L4 6 L3

=> d 14 1-6 ibib abs hitstr

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:631913 CAPLUS
DOCUMENT NUMBER: 135:195556
TITLE: Preparation of azolylphenyl oxamides as inosine monophosphate dehydrogenase (IMPDH) inhibitors
INVENTOR(S): Broadhurst, Michael John; Hill, Christopher Huw; Hurst, David Nigel; Jones, Philip Stephen; Kay, Paul Brittain; Kilford, Ian Reginald; Mckinnell, Robert Murray
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: Eur. Pat. Appl., 256 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| EP 1127883 | A2 | 20010829 | EP 2001-103521 | 20010216 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| NO 2001000900 | A | 20010827 | NO 2001-900 | 20010222 |
| CN 1310179 | A | 20010829 | CN 2001-104906 | 20010223 |
| JP 2001261663 | A2 | 20010926 | JP 2001-51064 | 20010226 |
| PRIORITY APPLN. INFO.: | | | GB 2000-4392 | A 20000224 |
| | | | GB 2000-15877 | A 20000628 |
| | | | GB 2000-20322 | A 20000817 |



Thus, 1,1-dimethyl-3-(4-nitrophenoxy)propylamine (prepn. given) was coupled with N-[3-methoxy-4-(5-oxazolyl)phenyl]oxamic acid in the presence

of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide and 1-hydroxy-7-azabenzotriazole to give N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-(1,1-dimethyl-3-(4-nitrophenoxy)propyl)oxalamide. Tested I inhibited IMPDH with IC50 = 0.010-0.277 .mu.M. I can be used for treating immune mediated

conditions or diseases, viral diseases, bacterial diseases, parasitic diseases, inflammation, inflammatory diseases, hyperproliferative vascular

diseases, tumors, and cancer.

IT 357181-06-7P 357181-92-1P 357182-28-6P
357182-29-7P 357182-30-0P 357182-31-1P
357182-32-2P 357182-33-3P 357182-34-4P
357182-35-5P 357182-36-6P 357182-37-7P
357182-38-8P 357182-39-9P 357182-40-2P
357182-41-3P 357182-42-4P 357182-43-5P
357182-44-6P 357182-45-7P 357182-46-8P
357182-47-9P 357182-48-0P 357182-49-1P
357182-50-4P 357182-51-5P 357182-52-6P
357182-53-7P 357182-54-8P 357182-55-9P
357182-56-0P 357182-57-1P 357182-58-2P
357182-59-3P 357182-60-6P 357182-61-7P
357182-62-8P 357182-90-2P 357183-04-1P
357183-07-4P 357184-40-8P 357184-66-8P
357184-76-0P 357184-78-2P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of azolylphenyl oxamides as inosine monophosphate dehydrogenase (IMPDH) inhibitors)

RN 357181-06-7 CAPLUS

CN Ethanediamide, N-[3-[4-(4-acetyl-1-piperazinyl)phenoxy]-1,1-dimethylpropyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)- (9CI) (CA INDEX NAME)

N

O --

MeO

NH

C = O

C = O

NH

Me - C - Me

CH₂CH₂

RN 357181-92-1 CAPLUS

CN Ethanediamide, N-[2-(4-benzoyl-1-piperazinyl)-1,1-dimethylethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)- (9CI) (CA INDEX NAME)

N

O

MeO

NH

C=O

C=O

NH

Me-C-Me

CH₂

N

N

Ph-C
|
O

RN 357182-28-6 CAPLUS

CN Ethanediamide, N-[2-[4-(2,2-dimethyl-1-oxopropyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]- (9CI) (CA INDEX NAME)

N

O

MeO

NH

C=O

C=O

NH

Me-C-Me

CH₂

N

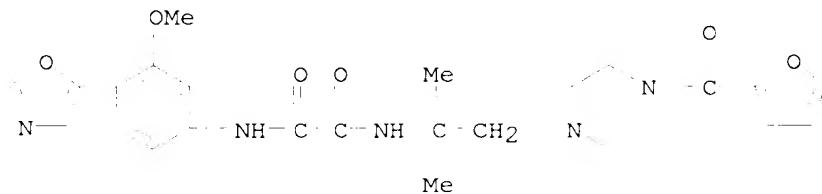
N

t-Bu-C

O

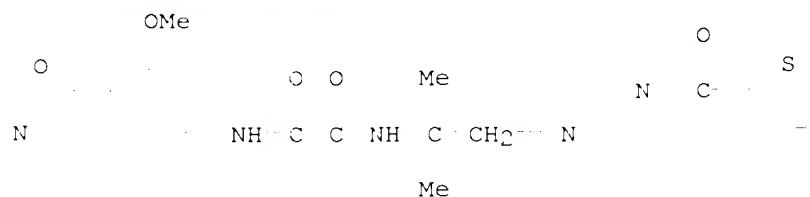
RN 357182-29-7 CAPLUS

CN Ethanediame, N-[2-[4-(2-furanylcarbonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]- (9CI) (CA INDEX NAME)



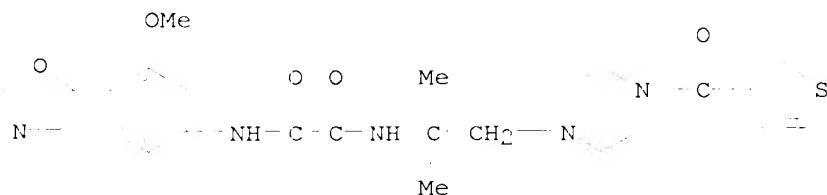
RN 357182-30-0 CAPLUS

CN Ethanediame, N-[1,1-dimethyl-2-[4-(2-thienylcarbonyl)-1-piperazinyl]ethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]- (9CI) (CA INDEX NAME)



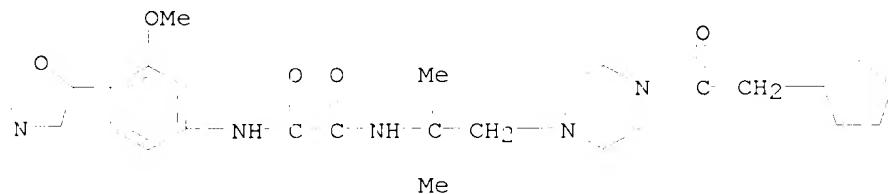
RN 357182-31-1 CAPLUS

CN Ethanediamide, N-[1,1-dimethyl-2-[4-(3-thienylcarbonyl)-1-piperazinyl]ethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)- (9CI) (CA INDEX NAME)



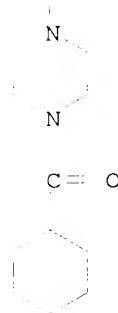
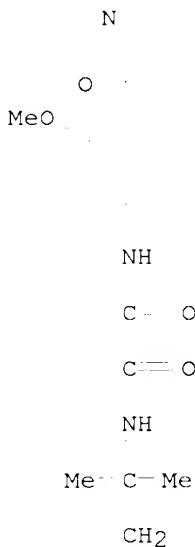
RN 357182-32-2 CAPLUS

CN Ethanediamide, N-[2-[4-(cyclopentylacetyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)- (9CI) (CA INDEX NAME)

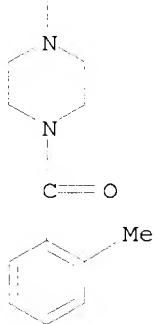
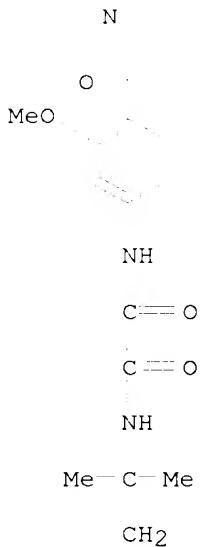


RN 357182-33-3 CAPLUS

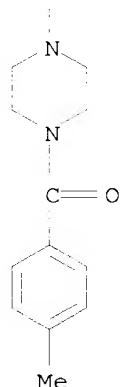
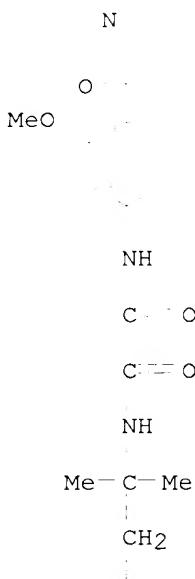
CN Ethanediamide, N-[2-[4-(cyclohexylcarbonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)- (9CI) (CA INDEX NAME)



RN 357182-34-4 CAPLUS
 CN Ethanediamide,
 N-[1,1-dimethyl-2-[4-(2-methylbenzoyl)-1-piperazinyl]ethyl]-
 N'-[3-methoxy-4-(5-oxazolyl)phenyl]- (9CI) (CA INDEX NAME)

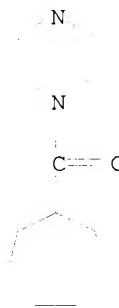
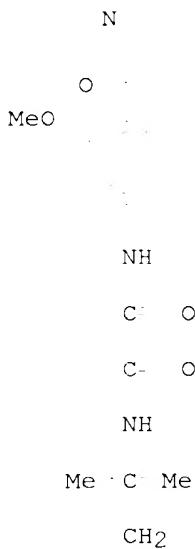


RN 357182-35-5 CAPLUS
 CN Ethanediamide,
 N-[1,1-dimethyl-2-[4-(4-methylbenzoyl)-1-piperazinyl]ethyl]-
 N'-[3-methoxy-4-(5-oxazolyl)phenyl]- (9CI) (CA INDEX NAME)

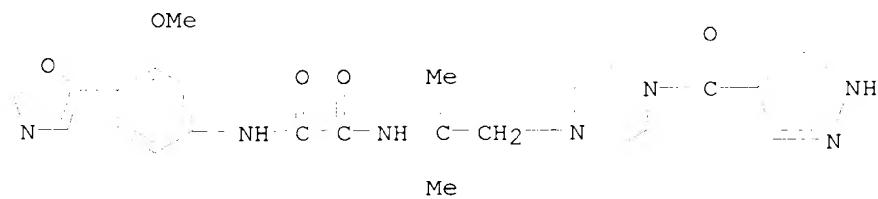


RN 357182-36-6 CAPLUS

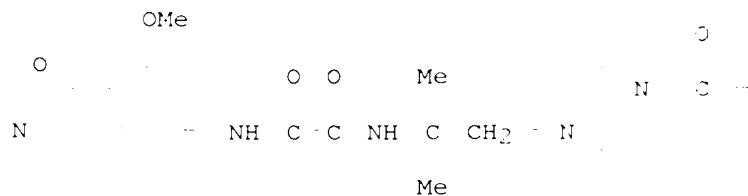
CN Ethanediamide, N-[2-[4-(cycloheptylcarbonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)- (9CI) (CA INDEX NAME)



RN 357182-37-7 CAPLUS
 CN Ethanediamide, N-[1,1-dimethyl-2-[4-(1H-pyrazol-4-ylcarbonyl)-1-piperazinyl]ethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]- (9CI) (CA INDEX NAME)



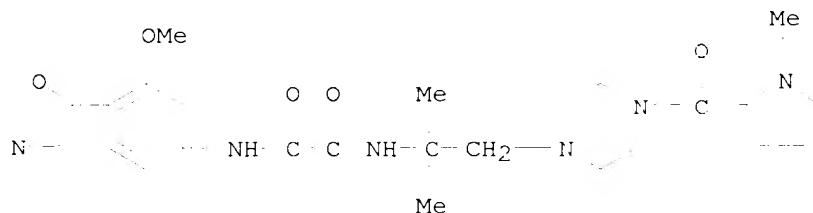
RN 357182-38-8 CAPLUS
 CN Ethanediamide, N-[2-[4-(cyclopentylcarbonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]- (9CI) (CA INDEX NAME)



RN 357182-39-9 CAPLUS

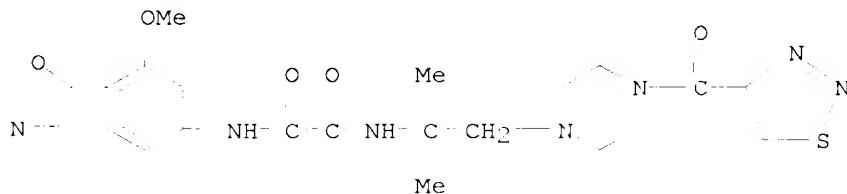
CN Ethanediamide,

N-[1,1-dimethyl-2-[4-[(1-methyl-1H-pyrrol-2-yl)carbonyl]-1-piperazinyl]ethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)- (9CI) (CA INDEX NAME)



RN 357182-40-2 CAPLUS

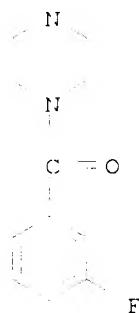
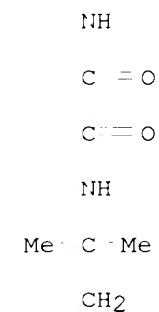
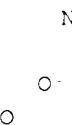
CN Ethanediamide, N-[1,1-dimethyl-2-[4-(1,2,3-thiadiazol-4-ylcarbonyl)-1-piperazinyl]ethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)- (9CI) (CA INDEX NAME)



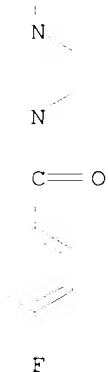
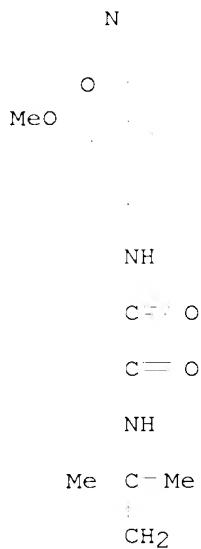
RN 357182-41-3 CAPLUS

CN Ethanediamide,

N-[2-[4-(3-fluorobenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl]- (9CI) (CA INDEX NAME)



RN 357182-42-4 CAPLUS
 CN Ethanediamide,
 N-[2-[4-(4-fluorobenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-
 N'-(3-methoxy-4-(5-oxazolyl)phenyl]- (9CI) (CA INDEX NAME)



RN 357182-43-5 CAPLUS

CN Ethanediamide, N-[2-[4-(cyclopropylcarbonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]- (9CI) (CA INDEX NAME)

N

O

MeO

NH

C=O

C=O

NH

Me C Me

CH₂

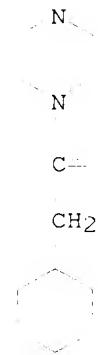
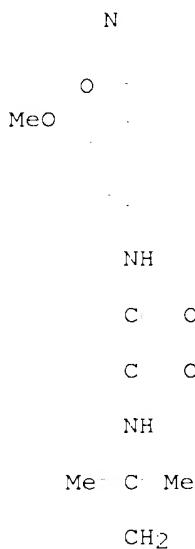
N

N

C=O

RN 357182-44-6 CAPLUS

CN Ethanediamide, N-[2-[4-(cyclohexylacetyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]- (9CI) (CA INDEX NAME)



RN 357182-45-7 CAPLUS
CN Ethanediamide, N-[2-[4-(3,3-dimethyl-1-oxobutyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)- (9CI) (CA INDEX
NAME)

N

O

MeO

NH

C O

C O

NH

Me—C—Me

CH₂

N

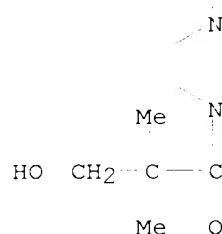
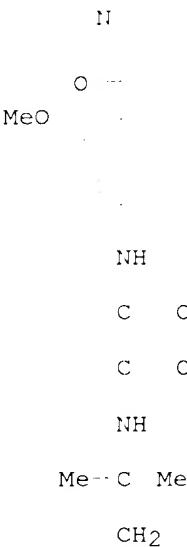
N

$$\text{Me}_3\text{C}=\text{CH}_2-\text{C}(\text{O})$$

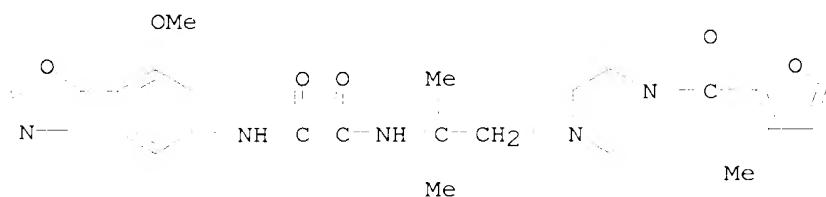
RN 357182-46-8 CAPLUS

CN Ethanediamide,

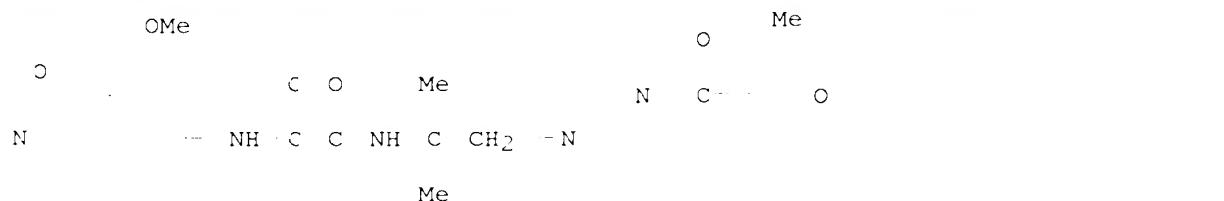
N-[2-[4-(3-hydroxy-2,2-dimethyl-1-oxopropyl)-1-piperazinyl]-
 1,1-dimethylethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)- (9CI) (CA INDEX
 NAME)



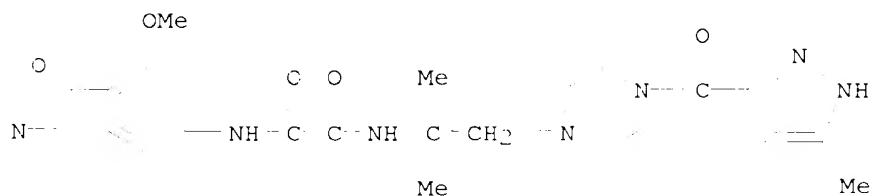
RN 357182-47-9 CAPLUS
 CN Ethanediamide, N-[1,1-dimethyl-2-[4-[(3-methyl-2-furanyl)carbonyl]-1-piperazinyl]ethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)- (9CI) (CA INDEX NAME)



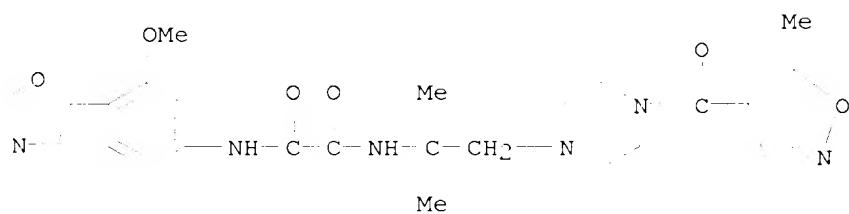
RN 357182-48-0 CAPLUS
 CN Ethanediamide, N-[1,1-dimethyl-2-[4-[(2-methyl-3-furanyl)carbonyl]-1-piperazinyl]ethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)- (9CI) (CA INDEX NAME)



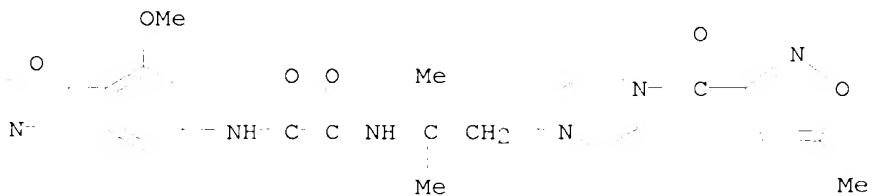
RN 357182-49-1 CAPLUS
 CN Ethanediamide,
 N-[1,1-dimethyl-2-[4-[(5-methyl-1H-pyrazol-3-yl)carbonyl]-1-piperazinyl]ethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)- (9CI) (CA INDEX NAME)



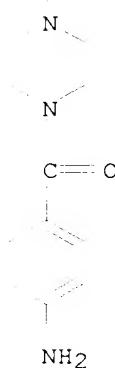
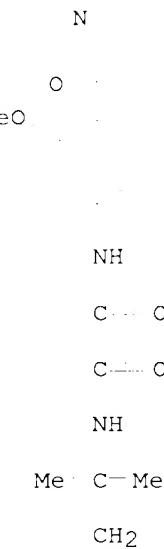
RN 357182-50-4 CAPLUS
 CN Ethanediamide, N-[1,1-dimethyl-2-[4-[(5-methyl-4-isoxazolyl)carbonyl]-1-piperazinyl]ethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)- (9CI) (CA INDEX NAME)



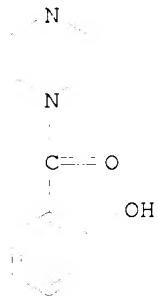
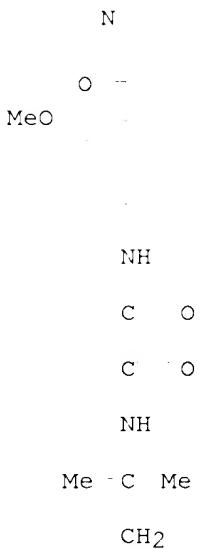
RN 357182-51-5 CAPLUS
 CN Ethanediamide, N-[1,1-dimethyl-2-[4-[(5-methyl-3-isoxazolyl)carbonyl]-1-piperazinyl]ethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)- (9CI) (CA INDEX NAME)



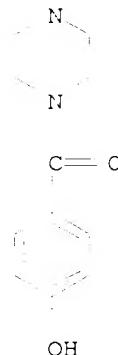
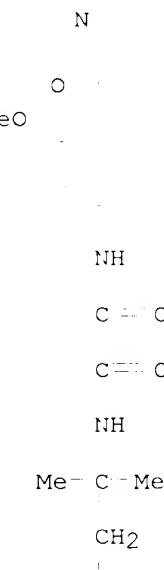
RN 357182-52-6 CAPLUS
 CN Ethanediamide,
 N-[2-[4-(4-aminobenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)- (9CI) (CA INDEX NAME)



RN 357182-53-7 CAPLUS
 CN Ethanediamide, N-[2-[4-(2-hydroxybenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]- (9CI) (CA INDEX NAME)



RN 357182-54-8 CAPLUS
 CN Ethanediamide, N-[2-[4-(4-hydroxybenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]- (9CI) (CA INDEX
 NAME)



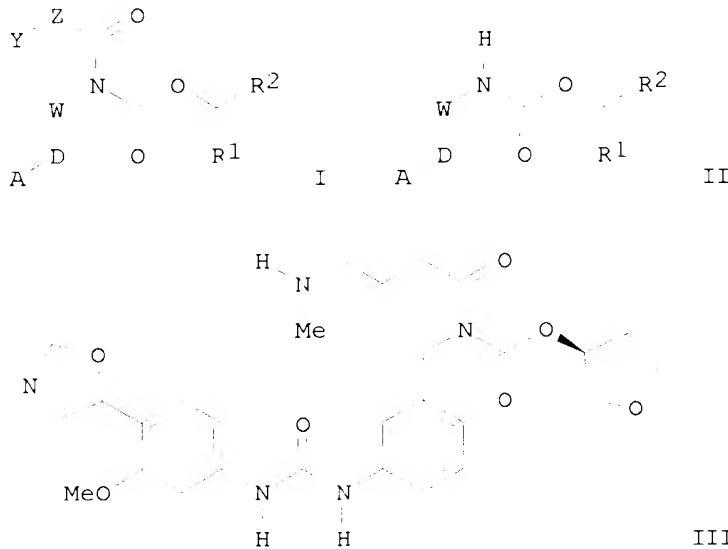
RN 357182-55-9 CAPLUS
 CN Ethanediamide, N-[2-[4-[(1,3-dimethyl-1H-pyrazol-5-yl)carbonyl]-1-piperazinyl]-1,1-dimethylethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)-(9CI)
 (CA INDEX NAME)

u
 RN 357182-57-1 CAPLUS
 => d 14 2-6 ibib abs hitstr

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:12455 CAPLUS
 DOCUMENT NUMBER: 134:86041
 TITLE: Preparation of carbamate prodrugs for inhibition of
 inosine monophosphate dehydrogenase (IMPDH)
 INVENTOR(S): Stamos, Dean P.; Bethiel, Randy S.

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
 SOURCE: PCT Int. Appl., 63 pp.
 CCDEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2001000622 | A1 | 20010104 | WO 2000-US17400 | 20000623 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MP, NE, SN, TD, TG | | | | |
| PRIORITY APPLN. INFO.: US 1999-141102 P 19990625 | | | | |
| OTHER SOURCE(S): MARPAT 134:86041 | | | | |
| GI | | | | |



AB Carbamate prodrugs I [W = (un)substituted monocyclic or bicyclic, (un)satd. or arom. ring system consisting of 5-6 members per ring (optionally heterocyclic); D = NR3CONR3, CONR3, NR3CO, NR3COCR4:CR4 where each R3 = H, (un)substituted alkyl, alkenyl or alkynyl; R4 = R3, (un)substituted alkyl, alkenyl or alkynyl attached via O, OCO, S, SO, SO2, SCO, NR3, or NR3CO; A = W, alkyl, alkenyl, or alkynyl where A optionally comprises up to 2 substituents wherein: the first of said substituents is R5 or W, and the second substituent, if present, is R5; R5 = (un)substituted 1,2-methylenedioxy, 1,2-ethylenedioxy, alkyl, alkenyl or alkynyl or (CH2)nW1; W1 = halo, CN, NO2, CF3, OH, alkoxy, etc.; n = 0-2; Y = NHR6; R6 = H, (un)substituted alkyl, alkenyl, alkynyl, aryl or alkylaryl and any NR6, taken together with the nitrogen and a carbon adjacent to the

nitrogen, optionally forms a 5-7 membered ring, wherein said ring optionally contains up to 3 addnl. heteroatoms; Z = (un)substituted alkyl, alkenyl, alkynyl, aryl-alkyl, -alkenyl or -alkynyl, wherein up to 3 carbon atoms may be replaced with O, S, SO, SO₂, or NR₆, wherein up to 3 CH₂ groups may be replaced with CO; R₁ = (un)substituted alkyl; R₂ = H, CF₃, alkyl, alkyl-W, W, or R₁ and R₂ together form a ring as defined in W], that on metab. convert to active inhibitors (formula II) of the IMPDH enzyme in vivo, were prep'd. Thus, III.cndot.HCl was prep'd. from methylaminobutyric acid in seven steps. I and pharmaceutical compns. thereof are particularly well suited for activation and subsequent inhibition of the IMPDH enzyme activity. The rate of absorption of I via oral uptake of the prodrugs was dependent on the nature of substituents Z and Y, as well as the pH, with AUC values ranging from <1 to 5 mg.cndot.hr/mL. Consequently, I may be advantageously used as therapeutic agents for IMPDH-mediated processes, e.g., cell proliferation (antitumor agents), and viral replication (antiviral agents).

IT 317345-64-5P 317345-66-7P 317345-68-9P
 317345-70-3P 317345-72-5P 317345-74-7P
 317345-76-9P

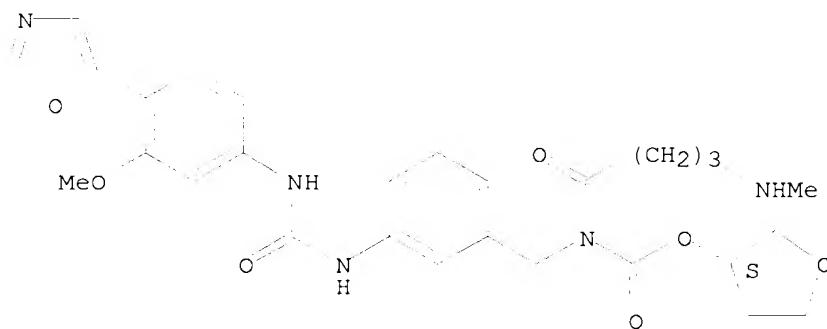
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses) (prepn. and biol. activity of N,N'-diphenylurea prodrugs of carbamate inhibitors of IMPDH)

RN 317345-64-5 CAPLUS

CN Carbamic acid,

[[3-[[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]carbonyl]amino]phenyl]methyl][4-(methylamino)-1-oxobutyl]-, (3S)-tetrahydro-3-furanyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



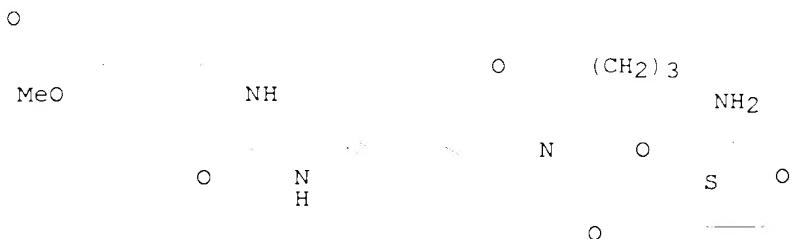
● HCl

RN 317345-66-7 CAPLUS

CN Carbamic acid, (4-amino-1-oxobutyl)[[3-[[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]carbonyl]amino]phenyl]methyl]-, (3S)-tetrahydro-3-furanyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

N

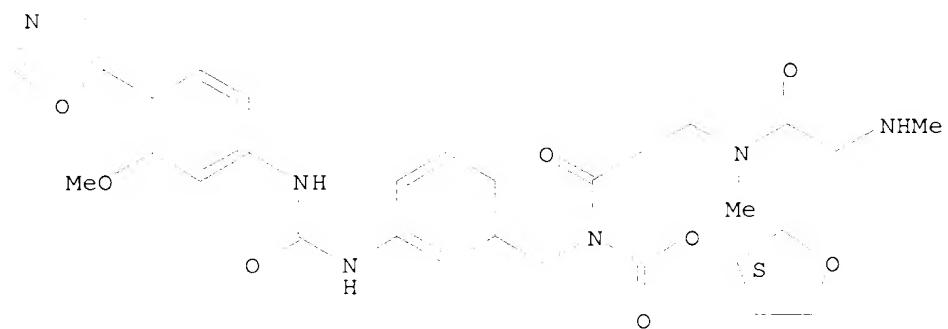


● HCl

RN 317345-68-9 CAPLUS

CN Glycinamide, N-methylglycyl-N-[[3-[[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]carbonyl]amino]phenyl]methyl]-N2-methyl-N-[[[(3S)-tetrahydro-3-furanyl]oxy]carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



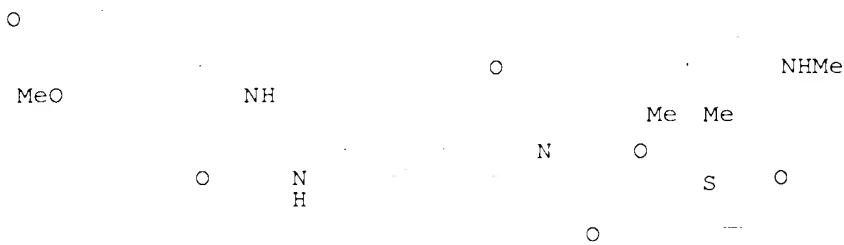
● HCl

RN 317345-70-3 CAPLUS

CN Carbamic acid, [3,3-dimethyl-4-(methylamino)-1-oxobutyl][[3-[[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]carbonyl]amino]phenyl]methyl]-, (3S)-tetrahydro-3-furanyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

N



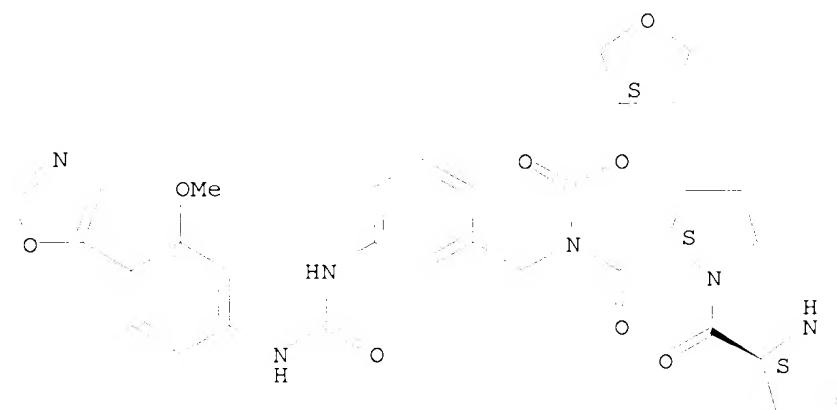
● HCl

RN 317345-72-5 CAPLUS

CN L-Prolinamide, L-prolyl-N-[[3-[[[[3-methoxy-4-(5-

oxazolyl)phenyl]amino]carbonyl]amino]phenyl]methyl]-N-[[[(3S)-tetrahydro-3-furanyl]oxy]carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

RN 317345-74-7 CAPLUS

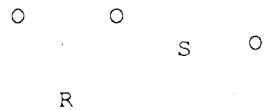
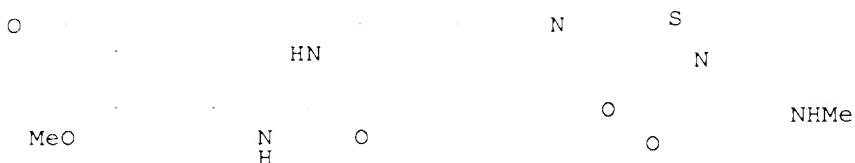
CN L-Prolinamide, N-methylglycyl-N-[[3-[[[[3-methoxy-4-(5-

oxazolyl)phenyl]amino]carbonyl]amino]phenyl]methyl]-N-[[[(3S)-tetrahydro-3-furanyl]oxy]carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

N

R



R

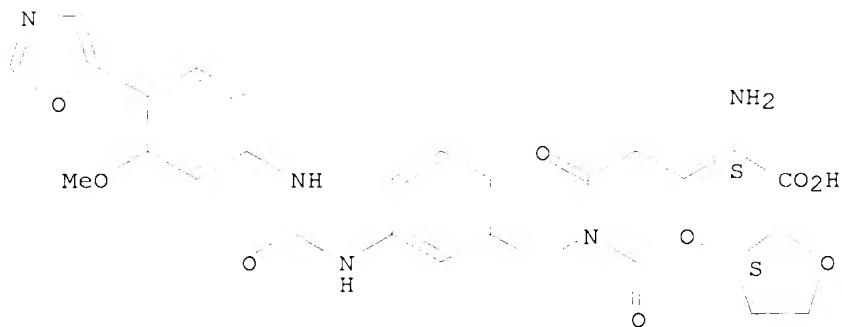
● HCl

RN 317345-76-9 CAPLUS

CN L-Glutamine,

N-[[3-[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]carbonyl]amino]phenyl]methyl-N-[[[(3S)-tetrahydro-3-furanyl]oxy]carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

IT 317345-62-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and biol. activity of N,N'-diphenylurea prodrugs of carbamate
inhibitors of IMPDH)

RN 317345-62-3 CAPLUS

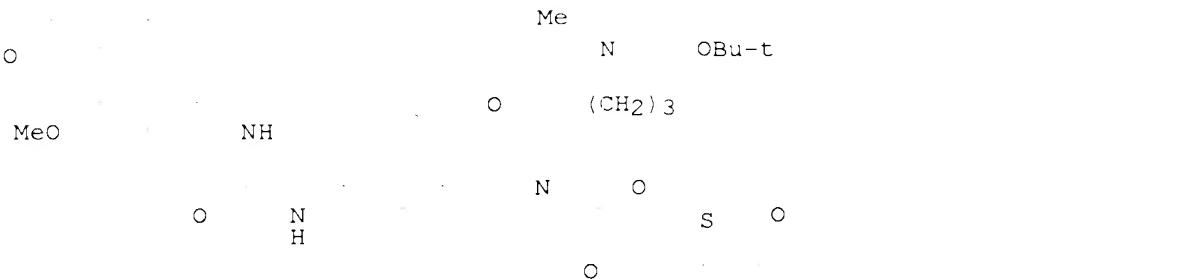
CN Carbamic acid, [4-[[[(1,1-dimethylethoxy)carbonyl]methylamino]-1-

oxobutyl] [[3-[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]carbonyl]amino]phenyl]methyl]-, (3S)-tetrahydro-3-furanyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

N

O



REFERENCE COUNT:

5

REFERENCE(S):
1988,

- (1) Beylin, V; JOURNAL OF HETEROCYCLIC CHEMISTRY V25(1), P97 CAPLUS
- (2) Kahns, A; 1991, 6, P483 CAPLUS
- (3) Kahns, A; INT J PHARM 1991, V71(1-2), P31 CAPLUS
- (4) Sharma, S; JOURNAL OF MEDICINAL CHEMISTRY 1989, V32(2), P357 CAPLUS
- (5) Vertex Pharmaceuticals Incorporated; WO 9740028 A 1997 CAPLUS

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:351518 CAPLUS

DOCUMENT NUMBER: 133:4650

TITLE: Preparation of heteroaryl-substituted aromatic compounds as antiherpes compounds

INVENTOR(S): Simoneau, Bruno; Crute, James J.; Faucher, Anne-Marie;

Grygon, Christine A.; Hargrave, Karl D.; Thavonekham, Bounkham

PATENT ASSIGNEE(S): Boehringer Ingelheim (Canada) Ltd., Can.

SOURCE: PCT Int. Appl., 157 pp.

CODEN: PIXXD2

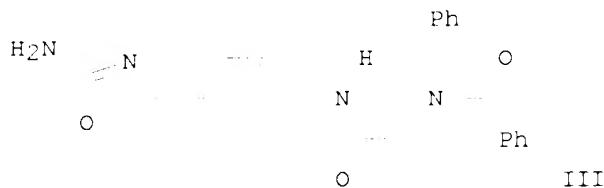
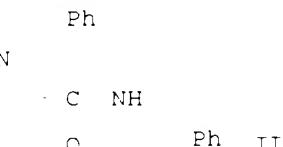
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|-----------------|-----------------|------------|
| WO 2000029399 | A1 | 20000525 | WO 1999-CA1066 | 19991109 |
| W: CA, JP, MX, US | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| PRIORITY APPLN. INFO.: | | | US 1998-108272 | P 19981112 |
| OTHER SOURCE(S): | | MARPAT 133:4650 | | |
| GI | | | | |



AB The title compds. X-Aryl-Y-Z [I; X = 5-6 membered arom. heterocycle; Aryl = (un)substituted Ph, pyridyl; Y is absent or a bridging group, for example $\text{NHC}(\text{O})\text{CH}_2$; Z is a terminal group, for example $\text{NHCO}_2\text{t-Bu}$ or II], which inhibit the herpes helicase-primase enzyme, rendering the compds. useful as antiviral agents, were prep'd. E.g., a multi-step synthesis of benzamide III was presented. Biol. data (IC50 and/or EC50 against HSV-1 and HCMV) for compds. I were given.

IT **270566-02-4P**

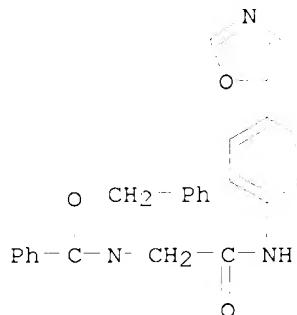
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of heteroaryl-substituted arom. compds. as antiherpes compds.)

RN 270566-02-4 CAPLUS

CN Benzamide,

N-[2-[[4-(5-oxazolyl)phenyl]amino]-2-oxoethyl]-N-(phenylmethyl)-
(9CI) (CA INDEX NAME)



REFERENCE COUNT:

5

REFERENCE(S):

- (1) Boehringer Ingelheim Ca Ltd; WO 9724343 A 1997 CAPLUS
- (2) Ciba Geigy Ag; EP 0045081 A 1982 CAPLUS
- (3) Sanofi Sa; FR 2754258 A 1998 CAPLUS
- (4) Spector, F; JOURNAL OF VIROLOGY 1998, V72(9), P6979 CAPLUS
- (5) Tularik Inc; WO 9942455 A 1999 CAPLUS

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:314682 CAPLUS

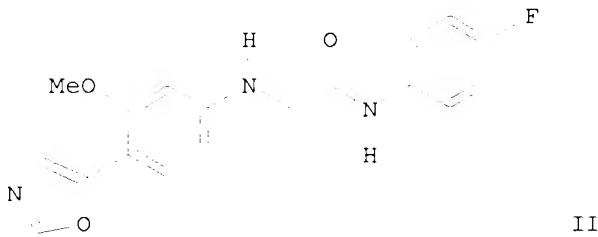
DOCUMENT NUMBER: 132:334449

TITLE: Preparation of N-[4-(5-oxazolyl)phenyl] amides as novel inhibitors of IMPDH enzyme

INVENTOR(S): Gu, Henry H.; Dhar, T. G. Murali; Iwanowicz, Edwin
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
 SOURCE: PCT Int. Appl., 99 pp.
 CCDEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|------------|
| WO 2000026197 | A1 | 20000511 | WO 1999-US24889 | 19991022 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
KE, KG, KP, KR, KW, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1127054 | A1 | 20010829 | EP 1999-960145 | 19991022 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO | | | | |
| PRIORITY APPLN. INFO.: | | | US 1998-106180 | P 19981029 |
| | | | WO 1999-US24889 | W 19991022 |

OTHER SOURCE(S): MARPAT 132:334449
 GI



AB The title compds. ZJKLX [I; Z = (un)substituted monocyclic or bicyclic ring system contg. up to 4 heteroatoms selected from N, O, and S; J = NR7, CO; K = NR7, CO, CHR9; L = a single bond, CO, CR10R11, etc.; X = alkyl, alkenyl, cycloalkylalkyl, etc.; R7 = H, alkyl, alkenyl, etc.; R9 = H, alkyl, alkenyl, etc.; R10, R11 = H, F, Cl, etc.], useful in treating or preventing IMPDH assocd. disorders, such as transplant rejection and autoimmune disease, were prep'd. E.g., a multi-step synthesis of gycinamide II was given. Compds. I are effective at 0.1-500 mg/kg/day.
 IT 267405-70-9P 267405-71-0P 267405-72-1P
 267405-73-2P 267405-74-3P 267405-75-4P
 267405-79-8P 267405-86-7P 267405-87-8P
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prep'n. of N-[4-(5-oxazolyl)phenyl] amides as novel inhibitors of IMPDH enzyme)
 RN 267405-70-9 CAPLUS
 CN Ethanediamide,
 N-[1,1-dimethyl-2-oxo-2-(1-piperidinyl)ethyl]-N'-(3-methoxy-

4-(5-oxazolyl)phenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

N

O

MeO

NH

C O

C=O

NH

Me-C-Me

C=O

PAGE 2-A

N

COO

RN 267405-71-0 CAPLUS
CN Ethanediamide, N-[1,1-dimethyl-2-(4-methyl-1-piperazinyl)-2-oxoethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl]- (9CI) (CA INDEX NAME)

N

O

MeO

NH

C = O

C = O

NH

Me - C Me

C = O

N

N

Me

RN 267405-72-1 CAPLUS

CN Ethanediamide,

N-[1,1-dimethyl-2-(4-morpholinyl)-2-oxoethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)-(9CI) (CA INDEX NAME)

N

O

MeO

NH

C = O

C = O

NH

Me - C Me

C = O

N

O

RN 267405-73-2 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[N-[3-methoxy-4-(5-oxazolyl)phenyl]-2-oxoglycyl-2-methylalanyl]-, ethyl ester (9CI) (CA INDEX NAME)

N

O

MeO

NH

C=O

C=O

NH

Me-C-Me

C=O

N

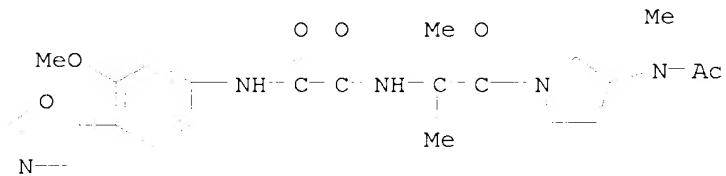
N

EtO C
|
O

RN 267405-74-3 CAPLUS

CN Ethanediamide,

N-[2-[3-(acetyl methylamino)-1-pyrrolidinyl]-1,1-dimethyl-2-oxoethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)-(9CI) (CA INDEX NAME)

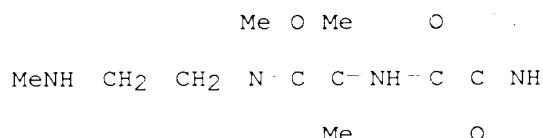


RN 267405-75-4 CAPLUS

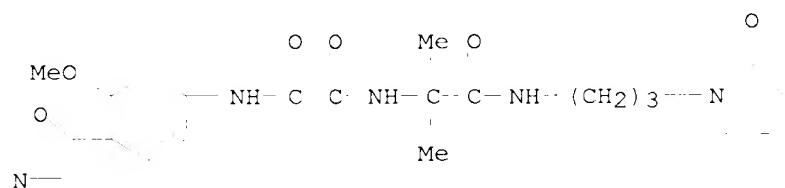
CN Alaninamide,

N-[3-methoxy-4-(5-oxazolyl)phenyl]-2-oxoglycyl-N,2-dimethyl-N-[2-(methylamino)ethyl]-(9CI) (CA INDEX NAME)

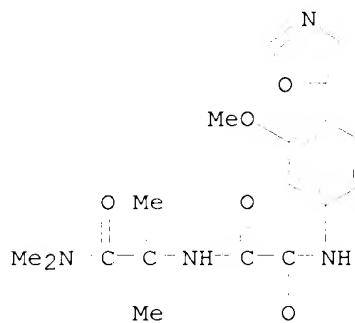
N



RN 267405-79-8 CAPLUS
CN Alaninamide,
N-[3-methoxy-4-(5-oxazolyl)phenyl]-2-oxoglycyl-2-methyl-N-[3-(2-oxo-1-pyrrolidinyl)propyl]- (9CI) (CA INDEX NAME)



RN 267405-86-7 CAPLUS
CN Alaninamide, N-[3-methoxy-4-(5-oxazolyl)phenyl]-2-oxoglycyl-N,N,2-trimethyl- (9CI) (CA INDEX NAME)



RN 267405-87-8 CAPLUS
CN Ethanediamide, N-[2-[4-(2-methoxyethyl)-1-piperazinyl]-1,1-dimethyl-2-oxoethyl]-N'-(3-methoxy-4-(5-oxazolyl)phenyl)- (9CI) (CA INDEX NAME)

N

O

MeO

NH

C=O

C=O

NH

Me-C=Me

C=O

N

N

CH₂-CH₂-OMe

REFERENCE COUNT:

3

REFERENCE (S):

- (1) Diana; US 4861791 A 1989 CAPLUS
- (2) Djuric; US 5073562 A 1991 CAPLUS
- (3) Goldstein; US 5334604 A 1994 CAPLUS

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:268526 CAPLUS

DOCUMENT NUMBER: 132:288797

TITLE: Inosine 5'-monophosphate dehydrogenase (IMPDH)

inhibitor preparation for therapeutic use

INVENTOR(S): Armistead, David M.; Badia, Michael C.; Bemis, Guy
W.;Bethiel, Randy S.; Frank, Catharine A.; Novak, Perry
M.; Ronkin, Steven M.; Saunders, Jeffrey O.

PATENT ASSIGNEE(S): Vertex Pharmaceuticals, Incorporated, USA

SOURCE: U.S., 22 pp., Cont.-in-part of U.S. 5,807,876.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|-------|-------|-----------------|-------|
| ----- | ----- | ----- | ----- | ----- |

| | | | | |
|---|----|----------|----------------|----------|
| US 6054472 | A | 20000425 | US 1997-832165 | 19970402 |
| US 5907876 | A | 19980915 | US 1996-636361 | 19960423 |
| WO 9740038 | A1 | 19971030 | WO 1997-US6623 | 19970421 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN,
YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| FW: GH, KE, LS, MW, SD, SE, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB,
GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN,
ML, MR, NE, SN, TD, TG | | | | |
| AU 9726785 | A1 | 19971112 | AU 1997-26785 | 19970421 |
| AU 723730 | B2 | 20000307 | | |
| EP 902782 | A1 | 19990324 | EP 1997-918759 | 19970421 |
| P: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO | | | | |
| CN 1219929 | A | 19990616 | CN 1997-194856 | 19970421 |
| BR 9708735 | A | 19990803 | BR 1997-8735 | 19970421 |
| JP 2001509132 | T2 | 20010710 | JP 1997-538234 | 19970421 |
| NO 9804917 | A | 19981223 | NO 1998-4917 | 19981022 |
| KR 2000010580 | A | 20000215 | KR 1998-708454 | 19981022 |
| PRIORITY APPLN. INFO.: | | | | |
| US 1996-636361 A2 19960423 | | | | |
| US 1997-801780 A2 19970214 | | | | |
| US 1997-832165 A 19970402 | | | | |
| WO 1997-US6623 W 19970421 | | | | |

OTHER SOURCE(S): MARPAT 132:288797

AB The invention relates to a novel class of compds. which are IMPDH inhibitors. This invention also relates to pharmaceutical compns. comprising these compds. The compds. and pharmaceutical compns. of the invention are particularly well suited for inhibiting IMPDH activity and consequently may be used as therapeutic agents for IMPDH-mediated processes. The invention also relates to methods for inhibiting the activity of IMPDH using the compds. of the invention and related compds.

IT 198821-00-0P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(inosine monophosphate dehydrogenase inhibitor prepn. for therapeutic use)

RN 198821-00-0 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[3-[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]carbonyl]amino]phenyl]-N-methyl- (9CI) (CA INDEX NAME)

N

O

MeO

NH

C O

NH

N-C-CF₃

Me O

IT 198820-96-1 198821-11-3

RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(inosine monophosphate dehydrogenase inhibitor prepn. for therapeutic
use)

RN 198820-96-1 CAPLUS

CN Acetamide,

N-[3-[[[[3-chloro-4-(5-oxazolyl)phenyl]amino]carbonyl]amino]phe
nyl]-2,2,2-trifluoro-N-methyl- (9CI) (CA INDEX NAME)

N

O-

Cl

NH

C=O

NH

N-C-CF₃

Me O

RN 198821-11-3 CAPLUS

CN Acetamide,

N-[3-[[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]carbonyl]amino]ph
enyl]-N-methyl- (9CI) (CA INDEX NAME)

N

O

MeO

NH

C O

NH

N-- AC

Me

REFERENCE COUNT:

13

REFERENCE(S):

- (1) Anon; US 4048333 1977 CAPLUS
- (2) Anon; WO 9401105 1994 CAPLUS
- (3) Anon; WO 9412184 1994 CAPLUS
- (4) Anon; US 5380879 1995 CAPLUS
- (5) Anon; US 5444072 1995 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:717901 CAPLUS

DOCUMENT NUMBER: 128:3680

TITLE: Preparation of arylreas and related compounds as inhibitors of inosine 5'-monophosphate dehydrogenase.

INVENTOR(S): Armistead, David M.; Badia, Michael C.; Bemis, Guy

W.;

Bethiel, Randy S.; Frank, Catharine A.; Novak, Perry M.; Ronkin, Steven M.; Saunders, Jeffrey O.

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Inc., USA

SOURCE: PCT Int. Appl., 93 pp.

CODEN: PIKKD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|--|----------|-----------------|----------|
| WO 9740028 | A1 | 19971030 | WO 1997-US6623 | 19970421 |
| W: | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KH, MD, RU, TJ, TM | | | |
| RW: | GH, KE, LS, MW, SD, SE, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | |
| US 5807876 | A | 19980915 | US 1996-636361 | 19960423 |
| US 6054472 | A | 20000425 | US 1997-832165 | 19970402 |
| AU 9726785 | A1 | 19971112 | AU 1997-26785 | 19970421 |
| AU 723730 | B2 | 20000907 | | |
| EP 902782 | A1 | 19990324 | EP 1997-918759 | 19970421 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, | | | |

| | | | | |
|------------------------|----|----------|----------------|------------|
| IE, SI, LT, LV, FI, RO | | | | |
| BR 9708735 | A | 19990803 | BR 1997-8735 | 19970421 |
| JP 2001509132 | T2 | 20010710 | JP 1997-538234 | 19970421 |
| NO 9604917 | A | 19981223 | NO 1998-4917 | 19981022 |
| PRIORITY APPLN. INFO.: | | | US 1996-636361 | A 19960423 |
| | | | US 1997-801780 | A 19970214 |
| | | | US 1997-832165 | A 19970402 |
| | | | WO 1997-US6623 | W 19970421 |

OTHER SOURCE(S): MARPAT 128:3680

AB ANHDNHB [A = (substituted) alkyl, alkenyl, alkynyl; B = (unsatd.) (substituted) mono- or bicyclic ring contg. 1 to ≤ 4 heteroatoms; D = CO,

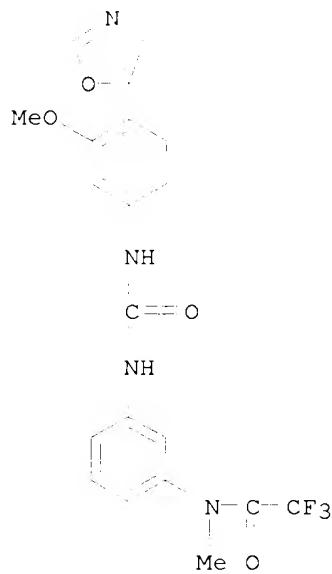
CS, SO₂], were prep'd. Thus, 4-(5-oxazolyl)aniline and PhCH₂NCO were stirred overnight in CH₂Cl₂ to give N-benzyl-N'-(4-(5-oxazolyl)phenyl)urea. Several title compds. inhibited IMPDH with $K_i = 0.01\text{--}50$ nM.

IT **198821-00-0P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arylreas and related compds. as inhibitors of IMP dehydrogenase)

RN 198821-00-0 CAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[3-[[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]carbonyl]amino]phenyl]-N-methyl- (9CI) (CA INDEX NAME)



IT **198820-96-1 198821-11-3**

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of arylreas and related compds. as inhibitors of IMP dehydrogenase)

RN 198820-96-1 CAPLUS

CN Acetamide,
N-[3-[[[[3-chloro-4-(5-oxazolyl)phenyl]amino]carbonyl]amino]phenyl]-2,2,2-trifluoro-N-methyl- (9CI) (CA INDEX NAME)

N

O
Cl

NH

C=O

NH

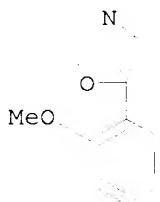
N-C-CF₃

Me O

RN 198821-11-3 CAPLUS

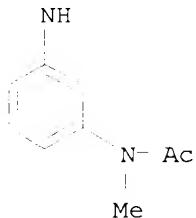
CN Acetamide,

N-[3-[[[3-methoxy-4-(5-oxazolyl)phenyl]amino]carbonyl]amino]phenyl-N-methyl- (9CI) (CA INDEX NAME)



NH

C=O



=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

| | | |
|--|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 40.79 | 181.48 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | -5.58 | -5.58 |

STN INTERNATIONAL LOGOFF AT 10:31:09 ON 15 JAN 2002